

Poster 22: Obese microenvironmental signaling and junctional protein disruption in endometrial cells: an early pro-oncogenic change?

Megan E. Ross, MD, MPH – University of Texas Health Science Center San Antonio

Topic: Endometrial

Objectives

The purpose of this study is to describe the impact of paracrine signaling of plasminogen activator inhibitor-1 (PAI-1) and interleukin-6 (IL-6) on endometrial epithelial junctional proteins in an obese microenvironment in order to gain insight into non-hormonal mechanisms of endometrial oncogenesis in the obese population.

Methods

Immortalized endometrial epithelial cells (EM-E6/E7/TERT) were cultured and treated with PAI-1 (0.5nM) and IL-6 (10ng/mL). Cells were assessed for changes in junctional complex gene transcription, protein expression, and cellular proliferation and migration, via quantitative real time polymerase chain reaction (qRT-PCR), Western blotting, and Incucyte-based functional assays of proliferation. Immunofluorescence (IF) staining and confocal microscopy were used to highlight changes in connexin 32 (Cx32) encoded by the gap junction gene GJB1. These experiments were repeated in another established endometrial epithelial cell line (hEM3).

Results

Transcription of GJB1 and corresponding protein connexin 32 (Cx32) levels were reduced when EME-E6/E7/TERT cells were treated with both PAI-1 and IL-6. This reduction in Cx32 levels with PAI-1 and IL-6 treatments was also seen in the hEM3 cells.

Conclusions

The decline of Cx32 levels in the setting of PAI-1 and IL-6 exposure indicates that PAI-1 and IL-6 contribute to important dysregulatory changes within the endometrial epithelial junctional complex proteins. This assertion is strengthened by concordant findings in a separate endometrial epithelial cell line. Reduction in Cx32 production has previously been associated with endometrial hyperplasia and carcinoma. The findings of this study link obesity-related paracrine signaling to this phenomenon, which provides further information about causality between obesity and endometrial cancer. More research is required to investigate if IL-6 or PAI-1 would serve as a suitable therapeutic target in the management of endometrial hyperplasia or malignancy in obesity.